Exhibit C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 1 PROLIFT CASES**	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

EXPERT REPORT OF JOSEPH CARBONE, M.D.

1. BACKGROUND AND QUALIFICATIONS

I am Board Certified in Urology and Female Pelvic Medicine and Reconstructive Surgery. I have been Medical Director of the Piedmont Institute of Continence and Urinary Control for 15 years. I began my medical training when I was accepted into the Washington University in St. Louis Scholars Program in Medicine as one of ten students selected in the country from high school into the Washington University in St. Louis School of Medicine. Upon completion of my undergraduate degree in Biochemistry and Philosophy, I completed training at the Washington University in St. Louis School of Medicine that has consistently been ranked as one of the top ten medical schools in the country. I was accepted into the Urology residency program there, which at the time was ranked as one of the top five programs in the country. In addition to studying prostate cancer surgery under Dr. William J. Catalona and endourologic surgery under Dr. Ralph V. Clayman, I participated with Dr. Carl G. Klutke in

some of the earliest experiences in the use of transvaginal mesh for the treatment of stress urinary incontinence in the United States. I personally met and discussed the technique with the late Dr. Ulf Ulmsten who has been credited with the original research on the suburethral transvaginal tension-free mesh in Europe. After completing my residency training, I was selected as one of two residents in the world into the UCLA fellowship in Neurourology, Urodynamics and Female Urology under the tutelage of female pelvic reconstructive surgeon, Dr. Shlomo Raz.

After training, I elected to pursue a career in a small-town private practice where those in need could get the greatest benefit from my training. It is there where I established the Piedmont Institute for Continence and Urinary Control and brought world-class care to a rural setting. I have maintained my skills through the performance of hundreds of suburethral mesh slings and various prolapse reconstructions including non-mesh and mesh techniques. When I was interested in studying the Prolift technique, I went to Lille, France to learn from Professor Michel Cosson, one of the original investigators in the European Transvaginal Mesh group. I brought my training back to the community in which I practiced and have successfully performed the technique without major complication.

I have shared my knowledge and training with the surgical community through my participation in the Ethicon preceptorship program. Through the years, I have provided education and training to hundreds of surgeons in the techniques of incontinence and prolapse repairs using the retropubic, obturator,

single incision and abbreviated obturator slings as well as the Prolift device. As I always explained at my presentations, the purpose of the training was to ensure the proper performance of the various techniques so that everyone could expect relatively uniform risks and outcomes rather than persuade anyone to adopt the techniques. They felt strongly and always stressed that choice of what surgery to perform was a decision between the surgeon and the patient based on a balance between the most recent and reliable scientific data available in the peer-reviewed literature and the patient's own personal opinions. The purpose of the preceptorship was to provide the surgeon with hands-on training or real-life experience with the technique of interest, while providing information on device usage, risks and complication avoidance and management. Thus, the most important step in the selection of the patient and technique for performing pelvic reconstructive surgery has been and will always be the clear and direct communication between the physician and patient through the objective process of informed consent.

2. INFORMED CONSENT

Informed consent is the process by which the treating health care provider discloses appropriate information to a competent patient so that the patient may make a voluntary choice to accept or refuse treatment.[1] It originates from the legal and ethical right the patient has to direct what happens to her body and from the ethical duty of the physician to involve the patient in her health care. First and foremost, accurate, adequate and relevant information must be provided truthfully in a form and language that the patient can understand. This is the primary

responsibility of the physician. It is the reason why we read peer-reviewed journals, attend CME conferences and keep our Specialty Certifications up-to-date. It is also the reason why the Prolift IFU recommends training on the use of the Prolift pelvic floor repair system. On the other hand, while the information provided to a patient should include all material risks, the list of risks and side effects cannot be exhaustive to the level of absurdity and impracticality.[2] What is expected is that the doctor should provide information that a prudent or reasonable patient would expect to make a knowledgeable decision about the course of action to be taken in the presence of alternatives.

What one must recognize, however, is that all interventions, including prolapse surgery, carry risk. This is the primary responsibility of the patient. Patients' perception of risk of a medical intervention is highly individualistic, variable and unpredictable. It is an element known only to the patient and must be respected by the physician. Patient should be given opportunity to ask questions and clarify all doubts. Similarly, patients have the responsibility to address these concerns either with their physician or another health care provider before acknowledging informed consent.

Only when both responsibilities are met can the process of informed consent be considered complete. This creates the setting in which a successful intervention for pelvic organ prolapse can be accomplished regardless of alternative chosen.

3. PELVIC ORGAN PROLAPSE (Background)

Pelvic organ prolapse (POP) occurs when female pelvic organs (such as the bladder, uterus, or rectum) fall into the vagina. This is typically caused by failure of the supporting structures in the pelvis. Risk factors include age, vaginal child birth, chronic heavy lifting or straining, smoking, obesity, loss of muscle tone, estrogen loss associated with menopause, family history, pelvic trauma or previous surgery, chronic constipation, chronic cough, and connective tissue disorders.

The exact prevalence of POP is difficult to ascertain due to the number of asymptomatic women with POP who do not seek medical attention. This distinction between asymptomatic and symptomatic POP is clinically relevant, since treatment is generally reserved only for women with symptoms. Population-based, questionnaire-driven studies have found that 6 to 8 percent of women report symptoms of POP.[3] These estimates underreport the true prevalence of POP, as surveys are likely to only identify women with advanced prolapse. The number of women who undergo surgical prolapse repair suggests a higher prevalence of POP. Population based studies report an 11 to 19 percent lifetime risk in women undergoing surgery for prolapse or incontinence.[4] Rates of asymptomatic POP are probably even higher. In the Women's Health Initiative study, the overall rates for prolapse in this population were 41 percent for women with a uterus and 38 percent post-hysterectomy. Anterior vaginal wall defects (33%) were significantly more common than posterior wall (18%) and apical defects (14%).[5]

Several factors in a patient's history predispose her to POP. The risk of POP increases with **parity**. In the Oxford Family Planning study, compared with nulliparity, the risk of hospital admission for POP increased 4-fold after the first birth, 8-fold after the second birth, 9-fold after the third birth and 10-fold after the fourth.[6] Fully 75% of prolapse can be attributed to pregnancy and childbirth among parous women.[7] Progressing **age** also plays a role. One study followed 1000 women between the ages of 18 and 83 annually and found that every additional 10 years of age conferred an increased risk of prolapse of 40%.[8] **Obesity** is a major factor in POP. Overweight and obese women (BMI >25) have a 2-fold higher risk of having prolapse than other women.[8] Prior pelvic surgery such as **hysterectomy** also increases risk.[9] It has been shown that Latina and Caucasian women were four- to five- fold higher to develop prolapse than African-American women.[10] Finally, there is weaker data suggesting that **chronic straining** with constipation[11] or occupations that involve **repeated heavy lifting**[12] can also contribute to the development of POP.

Traditional classification systems have categorized pelvic organ prolapse on a scale of 1 to 4 based on the lowest extent of protrusion in the standing and straining positions.[13] These categories are defined as follows: grade 1, mobility with straining, confined within the vagina; grade 2, mobility with straining, reaching the introitus; grade 3, mobility with straining, beyond the introitus; grade 4, mobility at rest beyond the introitus. While simple, this traditional grading system has been criticized with respect to both its reproducibility and the clinical significance of different grades.[14]

In 1995, a standardization document was introduced for the description, quantification, and staging of female pelvic organ prolapse and pelvic floor dysfunction.[14] While the particulars regarding obtaining the vaginal measurements are outside of the scope of this review, the POP-Q classification system which has been adopted by pertinent professional societies categorizes pelvic organ prolapse on a scale of 0 to 4 based on the lowest extent of protrusion in the standing and straining position. These stages are defined as follows: stage 0, no prolapse demonstrated with all points at -3 cm and the two superior vaginal points at –[TVL-2] cm; stage 1, the most distal portion of the prolapse does not extend beyond -1 cm; stage 2, the most distal portion of the prolapse is greater than -1 cm but less than +1 cm; stage 3 the most distal portion of the prolapse is greater that +1 cm but less than +[TVL-2] cm; stage 4, complete eversion with the most distal portion of the prolapse greater than +[TVL-2] cm. In addition, the POP-Q system considered the descriptive terms such as cystocele, rectocele, enterocele and urethrocele obsolete, since these terms implied an unrealistic certainty as to the structure on the other side of the vaginal bulge.

It is important to note that this marked the beginning of a paradigm shift away from the concept of isolated pelvic organ prolapse to a broader diagnosis of pelvic floor dysfunction. This diagnosis includes problems not only related to POP, but also stress urinary incontinence (SUI), chronic pelvic pain syndrome (CPPS) and sexual dysfunction (eg: dyspareunia). Clinicians and researchers alike now realize that these conditions are closely related with a common origin

of pelvic floor dysfunction. Similarly, treatments used to address these conditions have undergone a paradigm shift as well.

4. PELVIC ORGAN PROLAPSE (Non-Surgical Treatment)

Expectant management is a viable option for incidentally identified asymptomatic prolapse or women who are minimally bothered by their condition. However, women who decline treatment, particularly those with higher stage or symptomatic prolapse, run the risk of worsening pelvic organ prolapse or the development of associated pelvic floor dysfunction symptoms. These patients should be evaluated on a regular basis to assess for worsening prolapse or new onset urinary or defecatory problems, pelvic pain, and sexual dysfunction. In a study of 64 women with symptomatic prolapse who were followed for 16 months by sequential POP-Q exams alone, 20% had a > 2 cm increase in the leading edge of their prolapse and 40% desired to pursue further therapy due to the development of pelvic floor dysfunction symptoms. [15] In addition, on multivariate analysis there were no variables that could predict worsening prolapse or the development of pelvic floor dysfunction symptoms.

To mitigate the risks of expectant management, many advocate pelvic floor muscle training (PFMT). While it would seem inherently obvious that pelvic floor exercises should strengthen the pelvic floor, evidence supporting the benefits of such exercises for the treatment of pelvic organ prolapse has been scarce. In a recent Cochrane review, the authors concluded that only after six months of intense, individualized (one-to-one) PFMT was minor benefit in terms of anatomical and symptomatic improvement realized in the immediately post-

intervention period. Further evidence, however, relating to effectiveness of PFMT of different intensities in the medium- and long-term is needed.[16] Given that PFMT is rarely available in such an intense, individualized setting and that prolapse is a chronic condition, women that rely solely on PFMT as treatment for their POP run a high risk of treatment failure with worsening prolapse and the development of pelvic floor dysfunction symptoms in the long term.

One final non-surgical intervention that addresses the medium- and long-term management of pelvic organ prolapse is the use of a vaginal pessary. Since the days of 1550 BC when Ebers papyrus referenced "remedies to allow the womb of a woman to slip into its place," medicine has always sought to find a device that can be placed within the vagina to help support the prolapsed organ for the medium- to long-term. From wool plugs, to pomegranates dipped in lukewarm wine, to sponges wrapped in string, dipped in wax and covered with oil or butter, pelvic surgeons has striven to develop a device that supports prolapse in a manner that is effective, reliable and tolerable. Modern day pessaries are made of non-reactive silicone and come in various designs and sizes to suit each individual patient. Several studies have reported satisfaction and continued use rates of 60% in the short term (2-6 months)[17], 40% in the medium-term (1-2 years)[17] and up to 14% in the long-term (>10 years)[18]. Despite the clear long-term advantages over expectant management or PFMT alone, there are complications associated with the use of a vaginal pessary. Common complaints include pain, bleeding, discharge, odor and/or change in bladder or bowel function. More concerning are epithelial erosions and ulcerations. Over time,

these complications can lead to vesicovaginal and rectovaginal fistula, visceral obstruction with fecal impaction and/or hydronephrosis and urosepsis.[19] In a series of 2500 patients treated in France since 1971, 2.6% of cervical cancers and 30% of vaginal cancers occurred as a result of pessary use. Almost all tumors occurred at the site of contact and the mean time from insertion to diagnosis was 18 years. [20] Clearly, the use of a vaginal pessary is not without risk.

5. PELVIC ORGAN PROLAPSE (Surgical Treatment)

Surgical management of pelvic organ prolapse is often offered as a more definitive treatment for symptomatic patients. In a prospective cohort study of 680 women with symptomatic prolapse who were offered surgical v. non-surgical (pessary) treatment of their POP, women choosing surgery were younger (58 v 66) and perceived their prolapse as interfering with sexual satisfaction. They complained of more severe symptoms related to bowel or bladder emptying (often requiring digitation), lower abdominal pain, and vaginal "dragging". Overall, they focused much more on sexual function and quality of life. Nevertheless, it is interesting to note that in this study an overwhelming majority of 429 women chose the non-surgical option while only 251 women chose surgery.[21] Clearly, there is a high threshold of symptomatic "bother" to clear before a patient is willing to undergo surgery. Perhaps it is the acute understanding of the inherent risks of all prolapse surgery that gives women pause, regardless of the alternative chosen.

One of the most successful of all the surgeries for pelvic organ prolapse involves the open attachment of the vaginal apex to the anterior longitudinal

ligament of the sacrum just inferior to the sacral promontory. The abdominal sacrocolopexy (ASC) has evolved over time to provide support via a single graft strip, a cone around the vaginal apex, a double leaf graft, extension to the perineal body, or an elaborate 3 compartment mesh repair with extensive vaginal coverage. One of the greatest difficulties in assessing the success of traditional repairs is the multitude of variations on a theme that are all described under the same technique. A comprehensive review was attempted in 2004 to assess the outcomes following ASC. [22] Success rates averaged about 80% - 95% in the short to medium term of 6 months to 3 years. In the long term of 7 years, these success rates dropped to approximately 50%. [23] As expected, however, with success comes risk. Some of the common complications generally associated with surgery include infection (10.9%), hemorrhage (4.4%), ileus (3.6%), DVT/PE (3.3%) and incisional hernia (5.0%). Complications associated with pelvic surgery include cystotomy (3.1%), bowel injury (1.6%), and ureteral injury (1.0%). With regards to sexual dysfunction and dyspareunia, while the complaint declines from its preoperative incidence of 40%, the de-novo postoperative incidence is still 14%. [24] Finally, complications specific to ASC include injuries to the femoral, obturator, peroneal and/or sacral nerves, sacral osteomyelitis, and/or gluteal necrotizing myofascitis. In addition, when mesh is used to bridge the vaginal apex to the inferior sacral promontory, the risk of mesh erosion on long term (7 year) follow up is 10%. [23] While it is clear that the ASC offers excellent short and medium term success rates, the risks and morbidity associated with the

technique are high. It is not surprising that alterative approaches were developed to minimize the invasiveness of the ASC.

The two most popular apical support techniques utilizing a completely transvaginal approach are the uterosacral vaginal vault suspensions (ULS) and the sacrospinous ligament fixations (SSLF). As transvaginal operations, these approaches eliminated the large transabdominal dissection required of the ASC with lower risk of bowel or bladder injury, major hemorrhage or post operative ileus or bowel obstruction. Nevertheless, even these transvagainal approaches were not without unique risks. The ULS was known to cause ureteral occlusion in up to 11% of patients with 4% requiring reimplantation in one study.[25] In a review of the SSLF, the major complaint was buttock pain that occurred in 3% of subjects, although a vast majority resolved by 6 weeks postoperatively. Only severe pain radiating down the leg represented sciatic nerve entrapment requiring suture removal. [26] Unfortunately, the Achilles heel of these transvaginal techniques was the success rate. While the ASC enjoyed 95% success rate at 2 years,[27] the ULS and SSLF both had a success rate of only 60% at 2 years. [28] Thus, while the transvaginal approaches offered a lower complication rate, both in number and severity, the tradeoff was durability and success of the operation. Wound complications such as suture erosion and granulation tissue have been noted in 15-40% of cases.[29] Dyspareunia is a known risk as well and de novo dyspareunia rates of 26% have been reported for ULS and 36% for SSLF.[30]Colporrhaphy is another surgical technique to treat anterior and posterior

prolapse. High rates of recurrence of 30% or more have also been reported with colporrhaphy particularly in the anterior compartment.[31]

It was in this tradeoff that vaginally placed mesh for the treatment of pelvic organ prolapse found its niche. With the introduction of the TVT in 1998, tension-free Type 1 polypropylene mesh slings quickly became the gold standard for the treatment of stress urinary incontinence. This followed closely on the heels of the 1995 POP-Q standardization document for the description, quantification, and staging of female pelvic organ prolapse and pelvic floor dysfunction.[14] These changes combined to create a paradigm shift away from the concept of isolated pelvic organ prolapse to a broader diagnosis of pelvic floor dysfunction. This diagnosis includes problems not only related to POP, but also stress urinary incontinence (SUI), chronic pelvic pain syndrome (CPPS) and sexual dysfunction (eg: dyspareunia). Clinicians and researchers alike now realized that these conditions are closely related with a common origin of pelvic floor dysfunction. Similarly, treatments used to address these conditions underwent a paradigm shift as well.

It was well known by the turn of the century that reinforcement of traditional hernia operations with surgical mesh resulted in a lower failure rate of the repair. Three-year cumulative failure rates among patients who had suture repair and those who had mesh repair for primary hernias were 43 percent and 24 percent, respectively. For repair of a first recurrence of hernia, the failure rates were 58 percent and 20 percent, respectively.[32] Faced with a similar challenge, transvaginal pelvic surgeons began to “augment” their traditional pelvic organ

prolapse surgeries with mesh products in the 1990s to recreate an anatomically normal pelvic floor. At the time of surgery, the pelvic surgeon would trim a sheet of mesh and fashion it to lie on the repair. Attempts would be made to attach the mesh to supporting structures such as the sacrospinous ligament or the arcus tendineous fascia pelvis; however, these maneuvers proved challenging.

As an example, Flood and others published an article in International Urogynecology in 1998 entitled Anterior Colporrhaphy Reinforced with Marlex Mesh for the Treatment of Cystoceles.[33] This was a retrospective review of 12 years of experience with 142 patients; mean follow-up time of 3.2 years. They concluded that Marlex mesh used as reinforcement for anterior colporrhaphy was effective in preventing recurrent anterior wall descent with minimal complications.

In these early vaginal prolapse repairs, the only available mesh products were the same as those used by the general surgeons for abdominal surgery. In addition to the Marlex mesh used by Flood, PROLENE® polypropylene mesh had been in use for decades and was high burst strength knitted polypropylene monofilament mesh that was designed to retain strength indefinitely in clinical use.[34] Type 1 macroporous PROLENE polypropylene mesh has demonstrated optimal biocompatibility, efficacy, durability and safety in the TVT device to treat incontinence in its configuration of a 1.1 cm wide piece of mesh protected by a sheath and implanted transvaginally under the midurethra.[35] As the general surgeons evolved into the use of PROLENE® soft polypropylene mesh which was cleared in May of 2000, so did the pelvic surgeons for use in treating pelvic organ

prolapse. This Type 1 mesh offered a unique design that resulted in a mesh that was approximately 50% more flexible than standard PROLENE® polypropylene mesh with larger mesh pores.[36] In January of 2002, GYNEMESH PROLENE® soft polypropylene mesh was approved for pelvic floor repair. This approval validated the already exceedingly common use of the mesh for tissue reinforcement of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment was indicated. It is important to note this historical distinction. The manufacturer did not introduce the use of this material to the field of pelvic surgery. Rather, the pelvic surgeons themselves had been using mesh to treat prolapse for decades in ASC and for the transvaginal route, long before the approval of GYNEMESH PROLENE® soft polypropylene mesh for pelvic floor repair.

As an example of this distinction, in September 1998 Nicita published a paper called A New Operation for Genito-Urinary Prolapse.[37] Between January of 1996 and June of 1997 they used polypropylene mesh in a vaginal POP repair in 44 patients. They had good results but noted complications, including erosion and dyspareunia. They referred to the "fibrosis induced by the mesh" in a good sense, as reinforcement for pelvic structures. They concluded that the vaginal technique held promise for broad application.

The next step in the evolution of pelvic floor repair was to create a standardized, reproducible and reliable technique for the treatment of pelvic organ prolapse. Much like what the introduction of the tension free transvaginal tape procedure did for the treatment of stress urinary incontinence back in 1998,

investigators now sought a similar advancement in the treatment of pelvic organ prolapse.[38] After significant study, the likes of which were not seen previously for other manufacturers' prolapse devices, the GYNECARE PROLIFT® pelvic floor repair system was introduced in March of 2005. Using an ergonomically designed guide, cannula and retrieval device, the GYNECARE PROLIFT® pelvic floor repair system delivered precut GYNECARE GYNEMESH PS® polypropylene mesh to essentially recreate the normal anatomic pelvic floor. Again, this was in keeping with the paradigm shift away from isolated pelvic organ repair to pelvic floor reconstruction. Because the mesh provided not only the apical support of a SSLF but also lateral support to the arcus tendineous fascia pelvis (ATFP) and distal support to the bladder neck, the technique was recreating natural pelvic support rather than just "tacking" an organ. It held the promise of reproducibly and reliably offering the success rates of the ASC with the lower complication rates associated with the ULS or the SSLF.

In addition, because the GYNECARE PROLIFT® pelvic floor repair system was designed to be a standardized technique, a pelvic surgeon performing the procedure could expect relatively uniform risks and outcomes. No longer was the pelvic surgeon hindered by the multitude of variations on a theme that were all described under the same traditional technique. This standardization also allowed for the application of scientific investigation with randomized control trials (RCTs) offering Level 1evidence of outcomes. Since its inception, the GYNECARE PROLIFT® pelvic floor repair system has been involved in over 100 studies. In comparison, the traditional repairs, including the ASC, ULS and

SSLF were performed and modified for decades before ever being investigated in a single randomized control trial.

The success of vaginal mesh techniques, especially in the anterior compartment, has been proven in several RCTs. In a recent comprehensive review, the differences in success rates of vaginal mesh techniques compared to native vaginal tissue repairs were significant.[39]

Table 1 Randomised controlled trials comparing polypropylene mesh with traditional native vaginal tissue repairs

Reference	Total number patients	Follow up (months)	Compartment studied	Anatomic cure mesh (%)	Anatomic cure traditional (%)	*p*
Hiltunen et al. [9]	104	12	Anterior	93	62	<0.04
Sivaslioglu et al. [10]	90	12	Anterior	91	72	<0.05
Nieminen et al. [11]	105	24	Anterior	89	59	<0.05
Nguyen and Burchette [12]	75	12	Anterior	87	55	<0.05
Carey et al. [13]	139	12	Anterior Posterior	81	65.6	0.07
Nieminen et al. [14]	202	36	Anterior	87	59	<0.0001
Withagen et al. [15]	194	12	All	90	55	<0.001
Altman et al. [16]	389	12	Anterior	82	48	0.008
Sokol et al. [17]	65	12	All	38	30	0.45

After years of study, the conceptual advances in the surgical management of genital prolapse that resulted in the GYNECARE PROLIFT® pelvic floor repair system were beginning to achieve the success rates previously achieved only by the more invasive abdominal approaches such as the ASC. More recent Prolift studies continue to show significantly better cure rates compared to native vaginal tissue repairs as well as high levels of subjective improvements, patient satisfaction and quality of life.[40] The largest study, by Altman also showed statistically significant improvements in subjective cure assessed as sensation of bulging compared to native tissue and another recent large study showed significantly better cure, as well as prolapse quality of life scores, when compared to native tissue.[41]

6. COMPLICATIONS (Erosion/Exposure, Dysparunia, Contraction)

The complications associated with the GYNECARE PROLIFT® pelvic floor repair system compared to the more invasive approaches to pelvic organ prolapse repair were uncommon. Intraoperative rates of bladder perforation (3%), rectal perforation (1%), major hemorrhage (1%), and vaginal hematoma (2%) were all low.[42] Perioperative complications such as urinary retention (2%), anemia (1%), wound infection (1%), groin pain (2%), buttock pain (0%), fever (2%) and blood transfusions (1%) were also acceptably low. [43] There were no reports of ureteral injury, sacral osteomyelitis, and/or gluteal necrotizing myofascitis.

That is not to say, however, that there are no risks associated with the use of vaginal mesh for the treatment of pelvic organ prolapse. On the contrary, what one must recognize, is that all interventions carry risk. Regarding exposure, it has been argued by experts for Plaintiff that the GYNECARE GYNEMESH PS® polypropylene mesh used in the GYNECARE PROLIFT® pelvic floor repair system is in some way defective or not appropriate for use in the vagina. However, this argument is without support as earlier stated, wound complications such as suture erosions, wound hernia and dehiscence and granulation tissue formation occur at similar rates in non-mesh surgeries, and graft exposures occur at similar rates as well when used in prolapse surgery.[44]

Moreover, it has been shown that variation in surgical technique when performing vaginal mesh surgery is a much greater determinant of patient outcomes than are mesh properties or delivery systems. In one multicenter RCT

comparing trocar-guided mesh based repair to conventional repair involving 22 surgeons, the exposure rate ranged from 0% to 100%. [45] The same mesh and delivery system was used throughout the study. The only conclusion is that the wide variation in exposure rate is more of a function of variation in surgical technique. For transvaginal mesh procedures, this technique includes full-thickness vaginal wall dissection, careful and proper sizing, safe and accurate trocar placement, and proper mesh tensioning or setting. [46] All these are skills that were specifically and consistently addressed at the GYNECARE PROLIFT® pelvic floor repair system training programs. The GYNECARE PROLIFT® pelvic floor repair system instructions for use recommended and provided a means for arranging this training at no cost to the pelvic surgeon. The purpose of the training was to ensure the proper performance of the technique so that everyone could expect relatively uniform risks and outcomes rather than persuade anyone to adopt the technique.

As for the absolute risk of mesh exposure, the long-term risk for ASC utilizing mesh is 10% at 7 years. [23] Although there is one comparative trial reporting mesh exposure rates utilizing the vaginal approach comparable to those of ASC, [47] this study was investigating the laparoscopic approach to ASC rather than the traditional open approach.

Traditional vaginal approaches to pelvic organ prolapse repair utilize a "splitting" dissection, separating the vaginal epithelium from the underlying "vesicopelvic fascia." The pelvic surgeon then plicated this "fascia" to accomplish cystocele repair. Most experienced pelvic surgeons are very

comfortable and familiar with dissection in this plane. Placement of vaginal mesh for the repair of pelvic organ prolapse requires a full thickness incision, completely through the entirety of the vaginal wall. During dissection, gross visible perivesicle fat should be identified and followed to confirm entrance to the true vesicovaginal space. Again, all these are skills that were specifically and consistently addressed at the GYNECARE PROLIFT® pelvic floor repair system training programs. Improper placement of the GYNECARE GYNEMESH PS® polypropylene mesh, not any defect in the mesh itself or its "inappropriate" use in the vagina, was a key factor in the higher exposure rates reported in some studies associated with transvaginal mesh placement in the treatment of pelvic organ prolapse.

In addition, there are several patient-driven factors that increase the risk of wound complications following prolapse surgery, including mesh exposure. [48] Smoking, poorly controlled diabetes, early return to vaginal sexual activity, and non-compliance with estrogen supplementation has been noted as significant risk factors that are under the control of the patient. Younger age, more parities and concomitant hysterectomy are also factors, although the patient cannot modify them.

Regarding dyspareunia, it is important to note that in a prospective cohort study of 680 women with symptomatic prolapse who were offered surgical v. non-surgical (pessary) treatment of their POP, women choosing surgery were younger (58 v 66) and perceived their prolapse as interfering with sexual satisfaction. [21] In the ASC literature, the incidence of preoperative dyspareunia is

40%. The postoperative incidence of de novo dyspareunia drops to 14%. [24] These findings are in keeping with the paradigm shift from pelvic organ prolapse to the broader diagnosis of pelvic floor dysfunction, suggesting that dyspareunia is a part of the underlying problem rather than just a result of the intervention.

As for dyspareunia associated with the GYNECARE PROLIFT® pelvic floor repair system, one comparative study estimated the preoperative rate of dyspareunia at about 37 percent with the de novo post operative rate of about 17%. [49] This is in line with other pelvic organ prolapse surgeries including native tissue repairs:

TABLE 4
De novo dyspareunia after prolapse surgery

Dyspareunia	ASC N = 224 (148)[a] Handa et al[21]	SSLF N = 287 (106)[a] Maher et al[6]	USS N = 110 (34)[a] Silva et al[27]	APR N = 165 (81)[a] Weber et al[18]	Prolift N = 129 (57)[a]
Baseline (preop) dyspareunia (%)	40.5 (60/148)	Unknown	20.6 (7/34)	8.0 (6/81)	36.8 (21/57)
De novo (postop) dyspareunia (%)	14.5 (11/76)	36.1 (22/61)	25.9 (7/27)	19.0 (14/75)	16.7 (6/36)

[a] Number sexually active preop.

Lowman. Does the Prolift system cause dyspareunia? Am J Obstet Gynecol 2008.

Furthermore, in this same study, when the patients who had developed dyspareunia were surveyed, 94.7 percent responded that overall, the GYNECARE PROLIFT® pelvic floor repair system surgery had improved their quality of life and that they would have the surgery done again.

Dyspareunia is a long-standing, well-known complication that is well established in the surgical literature. Just as scars may result from incisions, all surgeons (not only pelvic surgeons) should reasonably understand that sexual dysfunction and pain may occur with vaginal surgery and convey that information to their patients preoperatively. Overall the studies comparing Prolift to native

tissue repairs do not show any statistically significant differences in rates of de novo dyspareunia, pelvic pain or sexual dysfunction. A recent evaluation of this subject in the Cochrane Review and by the Committee on the surgical management of pelvic organ prolapse for the 5th International Consultation on Incontinence showed that there were no significant differences in the rates of dyspareunia, de novo dyspareunia and sexual function between mesh and non-mesh prolapse repair.[50]

As regards the more controversial condition of mesh contraction, some still speculate as to the reality of its occurrence in vaginal mesh use. In one longitudinal study, 40 women were assessed at least twice, comprising almost 60 woman-years. Subjectively, approximately two-thirds (36) considered themselves cured or improved, while objectively one-third (16) had anatomic recurrence defined as cystocele stage 2 or greater. Utilizing translabial 4-dimensional ultrasound, the authors determined that the midsaggital mesh length actually ***increased*** significantly and the coronal mesh length also ***increased,*** although not significantly. [51] Moreover, the randomized controlled trials comparing Prolift and Gynemesh PS to native tissue repair do not show significant changes in vaginal length and caliber, nor do the other mesh versus native tissue studies.[52]

In addition, any surgeon familiar with surgical procedures and techniques involving pelvic floor repair and nonabsorbable meshes would know that the most fundamental principle for the use of vaginal mesh in recreating the normal pelvic floor is to make it tension free. This was clearly stated in the GYNECARE PROLIFT® pelvic floor repair system surgical technique manual when it was

written, "The straps should be used to make any required additional fine adjustment to the Total Implant position, taking care not to place the mesh under tension." This was the revolution that Dr. Ulmsten introduced to the world of stress urinary incontinence (SUI) treatment when he developed the tension free transvaginal tape procedure. Prior to the success of the TVT, a variety of synthetic meshes were attempted for the treatment of SUI (including polypropylene), all with unacceptable complications including erosion. [53] It was the introduction of the tension free principle that allowed the mesh to provide anatomic support without eroding through the tissues. Similarly, when placing the GYNECARE PROLIFT® pelvic floor repair system, final placement was expected to be in complete contact with the tissue, without folding or bunching and accomplished in a tension free fashion. Again, all these are skills that were specifically and consistently addressed at the GYNECARE PROLIFT® pelvic floor repair system training programs. If an appropriate tension free setting of the mesh was accomplished during surgery, even if mesh contraction were to occur, it would unlikely be clinically noticeable. If the mesh was placed under tension, folded, bunched or otherwise sub-optimally placed, then mesh contraction could conceivably cause erosion, dyspareunia or intractable pelvic pain. Regardless, this does not constitute a defect associated with the GYNECARE PROLIFT® pelvic floor repair system nor the GYNECARE GYNEMESH PS® polypropylene mesh. It does not demonstrate a lack of disclosure by Ethicon of the various concerns associated with their use. Rather, it represents known complications associated with the use of mesh anywhere in the

body that could be avoided by proper education that was made available by the manufacturer at no cost to the pelvic surgeon. Additionally, the instructions for use, professional education and Prolift Surgeon's Resource Monograph made it clear that scarring and contraction was a risk. Surgeons would know of the risks with prolapse surgery from their education, training, experience and the medical literature. The only unique risk with Prolift is mesh exposure and erosion, which would have been known to surgeons, as it is a wound complication like suture erosions in the past. Moreover, mesh exposure and erosion had long been discussed in the medical literature and were warned of in various materials such as the Prolift instructions for use, surgical technique guide, professional education, and the Prolift Surgeon's Resource Monograph.

In summary, Prolift has been demonstrated to be safe and effective. Longer term studies continue to show its efficacy and safety.[54] While there have been claims of the mesh roping and curling by experts of the Plaintiff, when placed according to the IFU and the arms detensioned the mesh will lie flat. Claims have been made regarding alternative meshes being better however, the overall data show that the Type 1 macroporous Prolene mesh in Gynemesh PS is suitable for use in pelvic organ prolapse and the mesh has been studied more and for longer follow up than others. The theory that an even larger pore and lighter weight mesh would be better has not shown to be true. One such mesh, Vypro, was studied by the TVM Group and found to not be tolerable.[55] Other meshes do not have a higher efficacy profile nor have the data shown them to be safer overall. There is still a risk of mesh exposure with the use of any mesh. As an

example, the rates of exposure with Prolift +M which uses Ultrapro mesh are not lower than the rates in Prolift which uses Gynemesh PS.[56] The data has demonstrated that both are suitable options to treat prolapse. Dyspareunia is always a risk with or without mesh and, as discussed earlier, the risk of dyspareunia, pelvic pain and sexual dysfunction with Prolift is no different than native tissue repairs. There have also been claims that the mesh degrades, is cytotoxic, leads to an adverse significant inflammatory response, and that it causes sarcoma formation or cancer. However, the clinical data is inconsistent with this theory as there are long-term studies of efficacy and safety. Additionally, the macroporous Prolene material has been studied in the body for up to 17 years showing its long-term biocompatibility. The data do not show a malignant risk.[57]

7. PROLIFT IFU

Instructions for use (IFU) accompany all medical devices like the Prolift. An IFU is not intended to serve as a comprehensive guide for a surgeon. Instead, it provides information about the device, the procedure, the indications, and warnings and precautions that the surgeon can use in conjunction with his or her training and experience. A reasonably prudent surgeon will be trained in pelvic floor surgery, with or without mesh, before he or she attempts to implant a Prolift. An IFU only supplements that training and experience.

The Prolift IFU adequately warned of all risks and potential complications associated with the Prolift. These risks were well known to the medical community.

8. PROLIFT PATIENT BROCHURES

Ethicon created patient brochures used to inform patients about Prolift. A patient brochure does not replace the patient-surgeon relationship or the related informed consent process. Prolift's patient brochures appropriately provide basic information to patients and recommend that she discuss her condition and options with her surgeon. Only a surgeon can determine, using his or her medical judgment, whether a particular patient is a candidate for Prolift.

9. PROLIFT PROFESSIONAL EDUCATION

Ethicon provides professional education to surgeons who desire such training. This professional education is not required for the purchase or implantation of Prolift. Instead, Ethicon provides optional learning opportunities through didactic lectures, cadaver labs, and hands on training with experienced surgeons. This training is not intended to replace a surgeon's formal medical training and experience. Instead, it is intended to supplement it with relevant and up to date information about a particular device and procedure. Ethicon's Prolift training was well planned, well executed, and goes beyond the industry standards for such training.

10. FDA PUBLIC HEALTH NOTIFICATIONS:

On October 20, 2008 the FDA issued a Public Health Notification to all healthcare practitioners regarding complications associated with the transvaginal placement of surgical mesh to treat Pelvic Organ Prolapse (POP) and Stress Urinary Incontinence (SUI). It read: "The most frequent complications included erosion through vaginal epithelium, infection, pain, urinary problems, and

recurrence of prolapse and/or incontinence. There were also reports of bowel, bladder, and blood vessel perforation during insertion. In some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia." [58] As of that date, all users familiar with surgical procedures and techniques involving pelvic floor repair and nonabsorbable meshes were put on notice as to the potential complications associated with these procedures such as the GYNECARE PROLIFT® pelvic floor repair system.

In addition, if they had not already done so, they should have followed the recommendation of the GYNECARE PROLIFT® pelvic floor repair system instructions for use and sought training on the use of the GYNECARE PROLIFT® pelvic floor repair system through contacting their company sales representative to arrange for this training. This training and the Prolift professional education supplemented the instructions for use. Had they done so, they would have learned about the transvaginal entrance into the vesicovaginal space utilizing a full thickness dissection through the vaginal wall thereby minimizing the risk of mesh exposure. They would have learned about setting the mesh so that it was completely in contact with the tissue without folding or bunching and, most importantly, without tension to minimize the risk of contraction, which surgeons would understand could cause erosion, dyspareunia or vaginal pain.

They would have also already been complying with the FDA safety communication of July 13, 2011. In it, the FDA warned that the serious

complications associated with surgical mesh for transvaginal repair of POP were not rare. They recommended that health care providers "obtain specialized training for each mesh placement technique, and be aware of the risks of surgical mesh." Notably, Ethicon had been offering professional education since 2005 on the Prolift. Also, although the FDA referenced contraction as a previously unidentified risk, Ethicon had been warning of scarring and contraction in their IFU and educational materials since 2005 and the medical literature had also reported scarring and contraction of the tissue as a risk of vaginal and prolapse surgery.[59] It is important to make one historical note at this time. What did not come out of the FDA safety communication of 2011 was any recall of any product related to the placement of surgical mesh for transvaginal repair of pelvic organ prolapse.

11. SUMMARY

The Prolift device has been extensively studied, more so than any other prolapse device. The clinical data and my personal experience show that it is safe and effective. Its design was state of the art and the macroporous type 1 Prolene polypropylene Gynemesh PS mesh was as well. The mesh has been shown to be biocompatible. Overall Prolift has high rates of cure, patient satisfaction, symptom resolution, and improvements in quality of life. All interventions carry risk. A complication does not mean that there is a defect. Native tissue prolapse repairs carry significant risks as well. The only unique risk with Prolift is mesh exposure and erosion, which has long been known to be a risk and was warned of in various materials such as the IFU, Surgical technique guide, professional

education and the Surgeons Resource Monograph. Studies show that mesh exposures and erosions are manageable, in many cases by conservative treatment. Mesh excision surgery is a simple procedure in our surgical repertoire and can be accomplished in the vast majority of cases easily and quickly. As surgeons we are trained on and have knowledge in managing wound complications, such as suture erosions, incisional herniation, biologic graft erosion, including surgery to treat these complications in non-mesh surgeries. There is always a risk of wound complications regardless of whether the procedure involves native tissue repair or the use of biologic graft or synthetic polypropylene mesh to treat prolapse. The large abdominal incisions as well as laparoscopic incisions can herniate, dehisce, or abscess. Risks of dyspareunia, pelvic pain, sexual dysfunction, tissue contraction and vaginal shortening have not been shown to be statistically significantly different between Prolift and native tissue. Moreover, many patients' pain and dyspareunia resolve after Prolift and sexual function and quality of life improve. Through specialized training available to any pelvic surgeon interested in learning more about the GYNECARE PROLIFT® pelvic floor repair system, any surgeon familiar with surgical procedures and techniques involving pelvic floor repair and nonabsorable meshes could have the opportunity to learn more about the techniques unique to the GYNECARE PROLIFT® pelvic floor repair system that would mitigate these risks. Ethicon made this education freely available to any surgeon interested in learning more about the GYNECARE PROLIFT® pelvic floor repair system or GYNECARE GYNEMESH PS® polypropylene mesh. While not required to do so, this education provided by

Ethicon informed surgeons of how to use the device, complications and complication management. The Prolift IFU, surgical technique guide, professional education, surgical videos, models, labs and Surgeons' Resource Monograph were exceptional and industry leading. Given the expected knowledge base of a pelvic floor surgeon performing prolapse surgeries, these materials were adequate for such a surgeon to accomplish successful prolapse repair with a minimum of risks and complications.

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